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Comparison of the effect of candida score and candida colonization index on decrease in candidemia incidence in our intensive care unit

Yoğun bakım ünitemizde kandida skoru ve kandida kolonizasyon indeksinin kandidemi insidansındaki azalmaya etkisinin karşılaştırılması

Abdullah Umut Pekok[1] Ahmet Yabalak[2] Sedef Tavukçu Özkan[3]
Metin Kement[4] Mehmet Pekok[5] Berfin Sude Pekok[6]

[1] İstanbul Aydin University Faculty of Medicine, VM Medical Park Pendik Hospital, Istanbul, Türkiye

[2] Düzce University Faculty of Medicine, Department of Neurology, Düzce, Türkiye

[3] VM Medical Park Pendik Hospital, Anesthesiology and Reanimation, İstanbul, Türkiye

[4] Bahçeşehir University Faculty of Medicine, Department of General Surgery, İstanbul, Türkiye

[5] Health Sciences University Gazi Yaşargil Training and Research Hospital, Department of Emergency Medicine, İstanbul, Türkiye

[6] Medical Faculty Student, Üsküdar University Faculty of Medicine, İstanbul, Türkiye

ABSTRACT

Aim: In this retrospective study, the effect of starting empiric treatment on the incidence of candidemia according to the candida score (CS) and candida colonization index (CCI) in patients followed in the intensive care unit (ICU) was investigated.

Materials and Methods: One hundred non-neutropenic adult patients aged 18-80 years old, hospitalized in the intensive care unit of our hospital, were included in the study. Cultures taken from patients hospitalized in the ICU between 01.06.2018 and 01.08.2021 were examined retrospectively. Swab samples were routinely taken from five main areas: mouth, nose, skin, perineum, and catheter, on the 7th day of each patient's hospitalization, to determine the CCI and CS. These samples were plated on Sabouraud dextrose agar (SDA) plates and the plates were incubated at 35 °C for 48 hours. The resulting yeast colonies were identified according to their microscopic appearance and biochemical properties. Fluconazole prophylaxis was initiated in patients with CS ≥3 or CCI ≥0.5. **Results**: A total of 500 culture samples from 100 non-neutropenic adult patients were analyzed (Average 5 cultures/patient). Seventy of the patients were male (70%), 30 (30%) were female and the average age was 71.5. While no growth was detected in any sample in 32 of a hundred patients (32%), growth was detected in at least one of the samples taken from 68 patients (68%), for a total of 118 samples. Of the yeasts, 104 were identified as Candida albicans, 10 as Candida glabrata, and 4 as Candida inconspicua. CS≥ 3 and CCI ≥0.5 were found in 11 (11%) patients, and CS≥3 and CCI<0.5 were found in 12 (12%) patients. Fluconazole prophylaxis was started in a total of 23 (23%) patients. No patient developed candidemia during their follow-up

Conclusion: These findings suggest that the evaluation of patients followed in the ICU with CCI and CS, and initiation of prophylactic treatment in patients who are found to be at risk may be effective in preventing possible fungal infections.

Keywords: Candida colonization index, candida score, incidence of candidemia, anti-fungal prophylaxis

Corresponding author: Abdullah Umut Pekok
Istanbul Aydin University Faculty of Medicine, VM Medical Park Pendik Hospital, Istanbul, Türkiye
E-mail: *umut.pekok@yahoo.com*
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ÖZ

***Amaç**: Bu retrospektif çalışmada, yoğun bakım ünitesinde (YBÜ) takip edilen hastalarda kandida skoru (KS) ve kandida kolonizasyon indeksine (KKİ) göre ampirik tedavi başlanmasının, kandidemi insidansına olan etkisi araştırıldı.*

***Gereç ve Yöntem**: Hastanemiz yoğun bakım ünitesinde yatan 18-80 yaş arası nötropenik olmayan yüz erişkin hasta çalışmaya dahil edildi. YBÜ'de, 01.06.2018 ile 01.08.2021 tarihleri arasında yatmış olan hastalardan alınan kültürler retrospektif olarak incelenmiştir. KKİ ve KS belirlemek için her hastanın hastaneye yatışının 7. gününde ağız, burun, deri, perine ve kateter olmak üzere beş ana bölgeden rutin olarak sürüntü örnekleri alındı. Bu numuneler Sabouraud dekstroz agar (SDA) plakalarına ekildi ve plakalar 35 °C'de 48 saat inkübe edildi. Elde edilen maya kolonileri mikroskobik görünümlerine ve biyokimyasal özelliklerine göre tanımlandı. KS ≥3 veya KKİ ≥0,5 olan hastalara flukonazol profilaksisi başlandı.*

***Bulgular:** Nötropenik olmayan yüz erişkin hastadan alınan toplam 500 kültür örneği incelenmiştir (Ortalama 5 kültür/hasta). Hastaların 70'si erkek (70%), 30'u (30%) kadın hasta olup yaş ortalaması 71,5 idi. Yüz hastanın 32'inde (%32) hiçbir örnekte üreme saptanmazken, 68 hastadan alınan (%68) örneklerden ise en az birinde olmak üzere toplam 118 numunede üreme oldu. Üreyen mayaların 104 tanesi Candida albicans, 10 tanesi Candida glabrata ve 4 tanesi Candida inconspicua olarak tanımlanmıştır. Onbir (%11) hastada KS≥ 3 ve KKİ ≥0,5, 12 (%12) hastada ise KS≥3 ve KKİ<0,5 saptandığı için toplam 23 (%23) hastaya flukonazol profilaksisi başlanmıştır. Takiplerinde kandidemi gelişen hasta olmamıştır.*

***Sonuç:** Bu bulgular, YBÜ'de takip edilen hastaların KKİ ve KS ile değerlendirilip riskli hastalarda profilaktik tedavi başlanmasının oluşabilecek fungal infeksiyonları engellemede etkili olabileceğini düşündürmektedir.*

***Anahtar Sözcükler:** Kandida kolonizasyon indeksi, kandida skoru, kandidemi insidansı, anti-fungal profilaksi*

INTRODUCTION

Candidas take fourth place as an infectious agent in intensive care units. Candida are found in the normal flora of the oropharynx and gastrointestinal tract. Many risk factors play a role in infections caused by candida. The most common among these risk factors is the patient's flora (1-3). Studies have shown that 90% of intensive care patients are colonized with Candida species (4). Invasive interventions in intensive care units, use of broad-spectrum antibiotics, advanced age, and immunosuppression or malignant diseases increase the incidence of candidemia (5, 6).

Candidemia is an important cause of mortality and morbidity in patients hospitalized in the intensive care unit (ICU). Therefore, various methods are used to identify high-risk patients and empirical anti-fungal therapy is recommended for these patients (3). Since the most important factor in the development of candidemia is the patient's flora, candida colonization should be accurately demonstrated. For this purpose, Candida colonization index (CCI) and Candida score (CS) scoring are recommended (7).

Empirical anti-fungal therapy is recommended according to the results of serological tests such as candida colonization index, candida score, and beta-glucan, especially in patients undergoing abdominal surgery and undergoing invasive intervention (8).

The aim of our study is to evaluate the effectiveness of the candida colonization index and candida score to prevent the development of invasive candidiasis in patients with risk factors for candidemia.

MATERIALS and METHODS

Ethics committee approval was received from Istinye University clinical research ethics committee on 23.06.2021, with decision number 2/2021.K-47. One hundred non-neutropenic adult patients aged 18-80 years old, hospitalized in the intensive care unit of our hospital, were included in the study. Patients with comorbidities at high risk of candidemia were included in the study. These risk factors were determined as central catheter application, total parenteral nutrition, malignancy, use of broad-spectrum antibiotics, and steroid use. Patients with at least 2 of these were included in the study. Patients with fewer

than two risk factors, patients younger than 18 years of age and older than 80 years of age, patients with a procalcitonin value>0.5, and growth detected in blood cultures were not included in the study. APACHE 2 and SOFA scores were used as scoring tools in all patients.

CCI is determined by dividing the number of anatomical regions sampled by the total number of samples taken (9). Candida score (CS), another scoring method, was determined by Leon et al. suggested by. CS is based on the scoring of 4 previously known independent risk factors (10). Sepsis was determined as 2 points, abdominal surgery 1 point, total parenteral nutrition 1 point and multifocal candida colonization 1 point and a value of ≥3 was accepted as a cut-off. In this way, the sensitivity was found to be 81% and the specificity to be 74%.

In the symposiums named "Advances in Antifungal Therapy" and "Transatlantic Controversies in the Management of Serious Fungal Infections" presented at the 11th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), it was recommended that surveillance cultures be made from five anatomical regions (11). Accordingly, in the intensive care unit of our hospital, swab samples are routinely taken from five main areas: mouth, nose, skin, perineum, and catheter, on the 7th day of each patient's hospitalization, to determine the CCI and CS (12-15). These samples are plated on SDA plates and the plates are incubated at 35 °C for 48 hours. The resulting yeast colonies are identified according to their microscopic appearance and biochemical properties. The CCI and CS of the patients are evaluated, and values of ≥3 for the CS and ≥0.5 for the CCI are accepted as the cut-off value.

In our ICU, prophylactic fluconazole treatment is started in patients who are found to be at risk. During the follow-up of all patients, it is monitored whether or not candida infection developed. Our study was conducted by retrospectively examining these samples.

Statistical Analysis

Data were analyzed by using SPSS version 20.0 for Windows. Results were given as percentages, mean and standard deviations, or median and ranges. Quantitative and qualitative variables were compared with Student's t-test and chi-squared (Pearson's or Fisher's exact) test, respectively. A P value of <0.05 was considered significant.

To calculate the CCI and CS, swab cultures were taken with sterile swabs from five areas of each patient's mouth, nose, skin, perineum and catheter, and then inoculated on SDA plates and incubated at 35°C for 48 hours. Yeast colonies formed on SDA were identified according to their microscopic and biochemical properties. The CCI and CS of the patients were evaluated, and values of ≥3 for the CS and ≥0.5 for the CCI were accepted as the cut-off value (10). Prophylactic fluconazole treatment was started in patients who were found to be at risk. During the follow-up of all patients, it was monitored whether or not candida infection developed.

RESULTS

Cultures taken from 100 adult patients followed in the intensive care unit between 01.06.2018 and 01.08.2021 were analyzed retrospectively. The APACHE 2 score of 100 patients was at least 14 and at most 25, and the average APACHE 2 score was 18.2. According to APACHE 2, the expected mortality rate was 29.13% and the actual mortality rate was 18.4%. The average SOFA score was found to be 2.2. Procalcitonin value was found to be <0.5 in all patients and there was no growth in blood cultures. In other words, there was no sepsis in the patients.

A total of 500 culture samples were taken from 100 non-neutropenic patients and analyzed (5 cultures/patient). There was no growth in any sample in 32 patients (32%), growth was detected in at least one of the samples taken from 68 patients (68%). Yeast colonies were detected in 118 (23.6%) of 500 samples. Of the 118 detected yeasts, 104 were identified as Candida albicans, 10 as Candida glabrata, and 4 as Candida inconspicua.

CCI and CS of the patients were evaluated. Values of ≥3 for CS and ≥0.5 for CCI were accepted as cut-off values (11).

In 11 patients (11%), CCI was higher than 0.5 and CS higher than 3. Although CCI was <0.5 in 12 patients, CS ≥3 was detected. The candida colonization indices and candida scores of all patients are given collectively (Table-1).

Prophylactic fluconazole treatment was given to 23 (23%) patients with CCI ≥0.5 or CS ≥3. The comparison of the CCI and CS cut-off values of the patients is also shown in Table-2.

During the follow-up, none of the patients developed candidemia.

Table-1. Collected results from patients.

Number of patients/Total number of cultures	CCI		CS	Fluconazole prophylaxis	Number of patients who developed IC
32/160	0/5	0	<3 (32 patients)	-	0
30/150	1/5=0.2	<0.5	<3 (30 patients)	-	0
27/135	2/5=0.4	<0.5	<3 (15 patients)	-	0
			>3 (12 patients)	+	0
10/50	3/5=0.6	>0.5	>3 (10 patients)	+	0
1/5	4/5=0.8	>0.5	>3 (1 patients)	+	0
0	5/5=1.0	0	0	-	0
100/500					

Candida Colonization Index (CCI): *Number of anatomical regions sampled / total number of samples taken*

Candida Score (CS): *Sepsis: 2 points, abdominal surgery: 1 point, total parenteral nutrition: 1 point, multifocal candida colonization: 1 point*

IC: Invasive Candidiasis

0.5 *is the cut-off value of CCI*

3 *is the cut-off value of CS.*

Table-2. Comparison of patients' CCI and CS cut-off values

	CS> 3		CS<3	
CCI> 0.5	11	patients	0	patient
CCI < 0.5	12	patients	77	patient

DISCUSSION

Candida are found in the flora of the gastrointestinal tract and oropharynx (2). Although there are many risk factors in infections caused by Candida species, it is known that the risk increases very much if there is Candida colonization in the endogenous flora (3, 16, 17). Candidemia occurs when Candida crosses the mucosal barrier and enters the blood. Therefore, it is recommended to start prophylactic antifungal therapy in patients with high colonization rates (18, 19).

In some studies, conducted in our country, it has been reported that candida colonization rates are high in intensive care units (20).

More than half of candidemia develop in ICUs. In a study conducted by Yapar et al., the incidence of candidemia in our country between 2000 and 2003 was found to be 0.24 per 1000 hospitalizations, and it was reported that 53% of these cases developed in intensive care units (2).

In a study by Çolak et al. (21), candida colonization was detected in 37 (92.5%) of 40 patients in the intensive care unit. In our study, candida colonization was detected in 68% of the patients.

In the EPIC II study, in which 1265 ICUs from 75 countries participated, 17% of nosocomial agents were found to be due to Candida, and the prevalence of candidemia was reported as 6.87 in 1000 ICU patients (6, 22).

In our study, we evaluated intensive care patients, the group in which candida infections are most common.

Delays in the diagnosis of candidemia and inadequate initial treatment are associated with high mortality (3). In a study, growth in blood cultures occurred after death in 41.2% of fatal candidemia cases (16). Therefore, early prophylactic anti-fungal therapy can be lifesaving in high-risk patients. Clinical scoring procedures and serological tests can be used to detect these high-risk patients (10).

In this approach, known as preemptive treatment, treatment is initiated if the CCI is ≥0.5, the CS is ≥3, or in the presence of fungal antigens such as 1-3-beta-D-glucan (23).

In our study, 1-3-beta-D-glucan and galactomannan antigens were not evaluated because they could not be studied in our hospital. Because serological tests such as 1-3 B D glucan, galactomannan and anti-mannan cannot be performed everywhere, it is not possible to study every patient because the results are late or expensive. Instead, it seems more appropriate in practice to study scoring systems such as CCI and CS because of their very low cost and quick results. In our study, we started prophylactic treatment in patients who were found to have CS ≥3 or CCI ≥0.5 by evaluating the CCI and CS of the patients.

In a study by Posteraro et al., they used the candida score due to the inability to perform serological tests such as beta-glucan and stated that it is an easy and effective method to be applied in patients (24).

Colonization means the risk of infection for many microorganisms (25). A CCI of ≥ 0.5 indicates a high risk of developing candidemia. The CCI reaches ≥0.5 on average 6 days before the development of candidemia. Therefore, CCI is valuable in identifying patients at risk for candidemia, initiating prophylactic anti-fungal therapy, and preventing the overuse of antifungals (26). In the CS, when the value of ≥3 is taken as a cut-off, its sensitivity was reported as 81% and specificity as 74%. It has been reported that the risk of candidemia increases 7.75 times when the CS is ≥3 (10).

In a prospective multicenter study to demonstrate the value of Candida score in distinguishing between colonization and candidemia in ICU patients, 1107 patients in 36 ICUs were included in the study. In this study, by evaluating the CCI and CS of the patients; CS ≥3, CCI was accepted as ≥0.5 cut-off value. Candida colonization was detected in 892 patients, and it was reported that ICU developed in 45 (13.8%) of 327 patients with CS ≥3 and 13 (2.3%) of 565 patients with a CS <3. The difference was found to be statistically significant. When evaluated according to CCI, it was reported that IC developed in 3.9% of those with a CCI of <0.5 and 8.7% of those with a CCI of ≥0.5. As a result, it has been reported that CS is better than CCI in predicting IC (27).

In our study, candida colonization was detected in 68% of 100 patients. Both CS ≥3 and CCI ≥0.5 were detected in 11 (11%) patients; Although CCI was <0.5, CS≥3 was detected in 12 (12%) patients and prophylactic treatment was given. This suggests that CS may be a more sensitive parameter than CCI.

We think that studying CS in all patients with CCI 2/5 will also be useful in deciding to start fluconazole prophylaxis. Invasive candidiasis did not develop in all of our patients. The lack of development of candidemia was attributed to the fact that the patients were not neutropenic and necessary hygienic precautions were taken and fluconazole treatment. The major limitations of our study are its retrospective nature and the absence of a control group that did not receive prophylactic treatment. There is a need for randomized controlled studies with a larger number of cases, including a control group.

CONCLUSION

As a result, it is possible to identify high-risk patients by evaluating with CS and CCI in non-neutropenic patients followed up in the intensive care unit, and to reduce the risk of candidemia and related mortality with prophylactic anti-fungal treatment in these patients. We think that CS is more sensitive in identifying more risky patients, and therefore, it may be more reliable to decide by calculating CS when starting prophylactic anti-fungal therapy. In addition, it is not possible to study every patient since serological tests such as 1-3 Beta D-glucan and anti-mannan, galactomannan cannot be performed everywhere, the results are delayed and expensive. Instead, it seems more appropriate in practice to study scoring systems such as CCI and KS in terms of very low cost and quick results.

Conflict of interest: The authors declare that they have no conflict of interest.

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